VICH/99/108
November 2000
Final

VICH Strategy and Work programme 2000 – 2005

INTRODUCTION

The VICH Steering Committee requested in October 1998 the development of a strategy, which would ensure more visibility and predictability in the overall VICH process.

At the 6th meeting in May 1999, the Steering Committee adopted the VICH Strategy document, which has been developed by T. Knox, with the help of Drs S. Thompson, P. Jones and C. Verschueren. A few minor amendments were included in August after the consultation on the final text.

At the same meeting, the Steering Committee requested the VICH Secretariat to develop a specific action plan for the practical implementation of the VICH Strategy. For purposes of completeness, the agreed Strategy is included as Part 1 of this document. The action plan proposed by the Secretariat is Part 2 of this document. The aim is to complete the Work Programme by 2005. However, the action plan timeframe will be reviewed by the Steering Committee on a regular basis. The titles of the action sections refer to goals as defined in the agreed strategy.

Part I: VICH Strategy

What is VICH?

VICH is a trilateral programme of collaboration between regulatory authorities and animal health industries of the European Union, Japan, and the United States of America, which aims to harmonize technical requirements for veterinary medicinal product registration within the 3 Regions. The regulatory authorities and animal health industries of Australia and New Zealand participate as observers, and the Office International Epizooties (OIE) participates as associate member in the VICH process. The full title of VICH is the "International Cooperation on Harmonisation of Technical Requirements for Registration of Veterinary Medicinal Products". VICH was officially launched in April 1996. The scope of the VICH programme includes both pharmaceutical and biological veterinary medicinal products.

Why was VICH set up?

A number of factors influenced the establishment of VICH including:

- the need to establish internationally acceptable requirements that ensure high standards of public and animal health are maintained,

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- the growing focus within OIE member countries on the need for effective regulation of veterinary medicinal products,
- the need to co-ordinate regulatory response to emerging global issues impacting on regulation of veterinary medicinal products,
- the desire to reduce the use of test animals by questioning the need for duplication of trials in each region,
- the need for increased efficiency in the use of regulatory resources, while ensuring the effectiveness of the regulatory systems,
- the international drive to harmonize regulatory standards and minimize their impact on trade,
- the desire to minimize the cost of gaining registration and facilitate the number of innovative products entering the market in the VICH regions,
- the desire to minimize variability in registration requirements between VICH regions which can lead to uncertainty, duplication and inconsistency and add considerable delays to product entry into the market,
- the desire to minimize regulatory timetables which can delay availability of new and innovative medicines much needed by veterinarians and animal owners,
- the need to minimize variability of testing methods which can lead to difficulties in comparing data within and between the VICH regions.

VICH was established under the auspices of OIE to respond to these factors by developing harmonized requirements for registration. The VICH Strategy and VICH's work programme form the basis of that response.

What does VICH aim to achieve?

The **Purpose of VICH** is to:

Establish harmonized regulatory requirements for veterinary medicinal products in the VICH Regions, which meet high quality standards, and minimize the use of test animals and costs of product development.

Provide a basis for wider international harmonization of registration requirements.

The specific aims of VICH are set out in the following **VICH Strategic Goals**:

Goal 1: **[By 2005], implement harmonized guidelines for all regulatory requirements where significant differences exist amongst the VICH members.**

Goal 2: **Contribute to the global response to significant emerging issues and science that impact on regulatory requirements within the VICH regions and/or adopted VICH guidelines.**

Goal 3: **Promote consultation and communication mechanisms that result in wider international awareness and acceptance of VICH guidelines.**

How will VICH go about achieving its aim?

VICH will adopt the following **VICH Guiding Principles** in pursuing its purpose and goals:

- VICH guidelines will be scientifically justified and will remove any unnecessary duplication of trials and requirements.
- VICH guidelines will facilitate transparent and consistent regulatory decision-making.
- wherever possible and appropriate, VICH guidelines will build on other available international guidelines, such as those developed by ICH, OECD and JECFA.
- the work of VICH will be designed to complement and not duplicate work being done by other international bodies, such as ICH, OECD and JECFA.
- proposed VICH guidelines will be widely consulted on internationally prior to adoption.

In order to achieve its purpose and goals, VICH has identified the following **Strategic Requirements** that will form the basis of its work programme:

Goal 1: [By 2005], implement harmonized guidelines for all regulatory requirements where significant differences exist amongst the VICH members.

1.1. Establish the process and procedures for development and implementation of VICH guidelines.

1.2. Identify and initiate work on VICH guidelines that will provide maximum immediate value to VICH members.

1.3. Identify potentially applicable guidelines and work being done by other international bodies that could form the basis for VICH guidelines.

1.4. Clearly define the long-term priority areas for development of VICH guidelines, based on the significance of existing differences in registration requirements amongst the VICH members.

1.5. Develop a long-term work programme for development of VICH guidelines, including definitive target dates for completion.

1.6. Implement formal mechanisms to evaluate the implementation of VICH guidelines, including assessment of the extent to which VICH's purpose and goals have been achieved.

Goal 2: Contribute to the global response to significant emerging issues and science that impact on regulatory requirements within the VICH regions and/or adopted VICH guidelines.

2.1. Ensure active communication between VICH members and observers to facilitate early identification of emerging issues and scientific findings within their regions.

2.2. Actively monitor the work programmes of other international organisations.

2.3. Develop and/or modify VICH guidelines to address significant emerging issues and new scientific findings which impact on regulatory requirements within the VICH regions.

Goal 3: Promote consultation and communication mechanisms that result in wider international awareness and acceptance of VICH guidelines.

3.1. Develop and promote a VICH website.

3.2. Profile the work of VICH in relevant international publications and conferences.

3.3. Liaise with other international bodies.

3.4. Hold regular VICH public conferences aimed at increasing awareness amongst regulatory officials, industry and the public both within and outside member regions.

3.5. Work with the OIE to facilitate the process of international consultation of proposed VICH guidelines.

How does VICH Function?

An **Organizational Charter of VICH** has been established which sets out the functions and modus operandi of the VICH programme. For further details, refer to the VICH website (http://vich.eudra.org).

Part II: Proposed Action Plan / Work Programme

I) VICH General organisation

1) Structure and functional aspects (Goal 1.1)

The overall structure, established in 1996, which has proven to be efficient, should be kept. In particular, the **following fundamentals should be maintained**:

- A well-functioning process as defined by the charter, additional guidance documents and SPOs
- Three active member regions (European Union – Japan – United States) plus an active ANZ observer (a de facto "quasi fourth member").
- One associate member, OIE, which has strongly supported the creation of VICH. OIE plays an essential role in the consultation phase and the dissemination of the information beyond those four regions; the future role of OIE within the VICH process needs however to be clarified.
- Interested Parties, which will be accredited to attend, but not participate in, Steering Committee meetings and will have to fulfil the requirements defined by the Steering Committee (VICH/00/117). Following a written request to the secretariat, Interested Parties shall be accredited on a permanent basis by the Steering Committee.
- A properly functioning secretariat with no policy role, but active in taking initiatives to make the process work efficiently (e.g. respect of deadlines, facilitation of consensus, drawing the attention of the members on issues, stimulation of work progress in-between meetings, etc.). The cost of the VICH secretariat is entirely absorbed by the COMISA budget. The COMISA Board is committed to continue current arrangements at this time, but can be expected to discuss the matter from time to time.
- Six active WG working simultaneously with the necessary flexibility for an additional one if necessary.
- The flexibility concerning the composition of Working Groups in relation to specific required expertise or to allow the participation of experts from outside of the three member regions
- The cost-effectiveness of meetings by continuing to have members hosting Steering Committee and Working Group meetings or taking charge of those meetings
- The meetings of Working Groups to be held in-between Steering Committee meetings (except during VICH conferences), although this should be improved (see below)

The Steering Committee does not see the need to make major changes to the structure and functional aspects of VICH. Nevertheless, the **scope of VICH** in relation to the following aspects might require alertness and eventually consideration:

- products that are generally considered as veterinary drugs (veterinary medicinal products) but are regulated by other regulatory agencies than those represented in VICH e.g. antibiotics administered as feed additives (EU), or ectoparasiticides (US)… Although the latter category of products was decided to be outside the work programme of VICH for the

time being, the scope of VICH should be kept flexible. Also, when initiating any new topic, the scope should be precisely defined in order to avoid later ambiguities such as those that have happened in the past, e.g. on GCP.

- aspects that would be the subject of other harmonisation processes such as mutual recognition agreements, but are now being considered (not yet started) in ICH, e.g. manufacturing requirements.

Action: Steering Committee

The efficiency of the VICH process, by way of a detailed questionnaire to all WG experts has been assessed. Based on this assessment, recommendations have been drafted on the ways to improve the appointment of experts and chairpersons/topic leaders to EWGs (VICH/00/152), on the ways to improve the information of new members to the expert working groups (VICH/00/150 and VICH/00/151), as well on the procedure to disband a EWG which has finished its task (VICH/00/153), on the procedure to ensure a broad consultation process at step 4 (VICH/00/154) and finally on the ways to support the EWG chairpersons in their efforts for the VICH process (VICH/00/155).

2) Liaison with ICH and other international bodies (Goals 2.2 & 3.3)

VICH should closely monitor the work achieved within **ICH** and take into account the ICH work plans. VICH should also identify potentially applicable guidelines and work being done by other **international bodies** that could form the basis for VICH Guidelines. Those identified by the secretariat are:

- **OIE**
- **OECD**
- **WAAVP** (for the Anthelmintics Guidelines)
- **JECFA**
- **CODEX**
- **WHO**

VICH should establish a mechanism to ensure a **permanent liaison** with the ICH secretariat in order to follow the progress of their specific issues. Since these are governmental organisations, **government members should support the secretariat** by establishing a regular contact channel between the secretariat and the relevant division(s) or person(s) within these organisations.

Action: Secretariat and Steering Committee

3) Timing of the SC meetings in relation to the WG meetings and calendar of such meetings *(Goals 1.1 & 1.5)*

The timing of Working Group meetings in relation with Steering Committee meetings has been discussed several times with various options being considered. However experience has shown that holding the Steering Committee and Working Group meetings in **alternance** is probably more cost-effective than if it would function, as in ICH, with huge parallel Steering Committee/Working Group session at the same time/same location. Indeed, VICH Steering Committee and Working Group meetings are held on a much smaller scale than in ICH and less Working Group meetings are necessary to arrive at a step 2 document because of fine-tuning work which takes place after the Working Group meetings.

In order to further improve the process of VICH, especially a smooth but time efficient progression through the steps of the (draft) guidelines, it is proposed to organise both Steering Committee and Working Groups meetings in a **fixed time frame**, leaving approximately 4 to 8 weeks between WG and SC meetings which will take place alternatively.

This will:

1. **Facilitate the experts task** by enabling them to **plan sufficiently in advance** their different working group activities

2. Enable the secretariat to **circulate the documents** sufficiently in advance of Steering Committee meetings
3. Enable Steering Committee participants to **review WG documents** (minutes, progress reports and draft VICH Guidelines)
4. Enable Steering Committee participants to better planning and **funding** of future VICH activities
5. Enable VICH Steering Committee participants and the Secretariat to make **plans for future work and better forecast of VICH results**.

Action: Steering Committee

Proposed schedule:

Meetings	**SC**	**WGs**	**SC**	**WGs**
2001	May	July	October	December
2002	April	June	September	November
2003	March	May	September	November
…..				

II) VICH Guidelines (Goals 1.2, 1.3, 1.4 and 1.5)

The future VICH work is divided in two parts: 1) on-going work (topics already selected by the SC and/or GL at various steps), and 2) potential future topics. In order to identify and initiate work on VICH Guidelines that will provide maximum value to VICH members (goal 1.2), all potentially relevant topics are laid down in the 2nd part hereunder. These are based on the VICH work programme established in July 1996 (document VICH/96/006), as well as on the proposals which have been forwarded during the last Steering Committee meetings and, in writing, by ANZ in September 1999.

Action: Steering Committee

1) On-going work (topics already selected by the SC and/or GL at various steps)

a) at step 2 and further

At step 7 – Guidelines already released and to be implemented by mid 2001 at the latest

- Environmental Impact Assessment (EIAs) for veterinary medicinal products (VMPs) Phase I
  VICH GL6 (Ecotoxicity - Phase 1) *(Implementation in Japan deferred until Phase 2 Guideline has been completed and adopted)*
- Efficacy of Anthelmintics: General Requirements
  VICH GL7 (Anthelmintics General)
- Stability Testing for Medicated Premixes
  VICH GL8 (Stability premixes)
- Good Clinical Practices
  VICH GL9 (GCP)
- Impurities in New Drug Substances
  VICH GL10 (Impurities New Substances
- Impurities in New Veterinary Medicinal products
  VICH GL11 (Impurities New VMPs)
- Efficacy of Anthelmintics : Specific Recommendations for Bovines
  VICH GL12 (Anthelmintics : Bovines)

- Efficacy of Anthelmintics : Specific Recommendations for Ovines
  VICH GL13 (Anthelmintics : Ovines) Draft 1
- Efficacy of Anthelmintics : Specific Recommendations for Caprines
  VICH GL14 (Anthelmintics : Caprines)
- Stability testing of biotechnological/biological veterinary medicinal products
  VICH GL17 (Stability: biotechnologicals/biologicals)
- Impurities: Residual Solvents
  VICH GL18 (Impurities: Residual Solvents)

At step 4 – Guidelines to be implemented by mid 2002 at the latest

- Efficacy of Anthelmintics: Specific Recommendations for Equine
  VICH GL15 (Anthelmintics: Equine)
- Efficacy of Anthelmintics: Specific Recommendations for Swine
  VICH GL16 (Anthelmintics: Swine)
- Efficacy of Anthelmintics: specific requirements for canine
  VICH GL 19 (Anthelmintics: canine)
- Efficacy of Anthelmintics: specific requirements for feline
  VICH GL 20 (Anthelmintcs: Feline)
- Efficacy of Anthelmintics: specific requirements for poultry
  VICH GL 21 (Anthelmintics : Poultry)
- Safety studies for veterinary drug residues in human food: reproduction studies
  VICH GL 22 (Safety: Reproduction)
- Safety studies for veterinary drug residues in human food: genotoxicity studies
  VICH GL 23 (Safety: Genotoxicity)
- Pharmacovigilance of Veterinary Medicinal Products: Management of Adverse Events Report (AERs)
  VICH GL 24 (Pharmacovigilance)

At step 2 – Guidelines to be implemented by mid 2002 at the latest

- Testing of residual formaldehyde
  VICH GL 25 (Biologicals)
- Testing of residual moisture
  VICH GL 26 (Biologicals)

b) At step 1

– Guidelines still to be developed and anticipated implementation in 2003 - 2004

- Target animal safety testing (Pharmaceuticals and biologicals)
- Safety testing
  1) first phase
     * additional studies to be carried out on a case-by-case basis, and
     * special studies required to refine the ADI for specific end-points
  2) second phase
     * establishment of toxicological end-points (ADI); risk assessment policy criteria
- Pharmacovigilance
  - Information Technology
- Environmental Impact Assessments (EIAs) for Veterinary Medicinal Products - Phase II
- Biologicals
  - Mycoplasma detection test method for Veterinary Biological Products
  - Extraneous virus test method for Veterinary Biological Products

- Specific requirements for antimicrobials pertaining to resistance
    - Design of studies (including pathogen load studies?) for the preapproval evaluation of antimicrobial resistance
    - Label recommendations related to the prudent use of antimicrobials
- General principles for the demonstration of safety
    - Required toxicity studies (as one comprehensive of requirements? vs. separate guidelines?):
        - Acute toxicity
        - Sub-chronic and chronic toxicity testing requirements
        - Assessment of the impact of residues on human gut flora
        - Reproduction toxicity
        - Teratology
        - Carcinogenicity/chronic toxicity

2) Potential future topics to be considered by the SC

The following list should be considered as a proposal that was set up in November 2000. The Steering Committee can amend this list at any time in particular by adding further new topics to the list:

- Biological topics *(Could probably be dealt with by the **existing** Working Group)*:
    - Inactivation testing and in vitro testing for killed products
    - Validation of potency tests
    - Test on the dissemination of the organism in the body and on reversion to virulence
    - Master seeds (characterisation, use of in vitro testing, release titre requirements)
    - Requirements for cell lines and primary cells
    - Stability testing
- Metabolism and residues kinetics

  Data requirements for residues of veterinary medicines in human foods, required by the regulatory authorities for them to set maximum residue limits and/or for their assurance that set limits are not exceeded, vary between countries. So is the willingness to accept data generated outside their own country.

  Priority for harmonised Guidelines *(Would probably require a **new** Working Group)*:
    - Protocols for residue studies
    - Guidance on interpretation of studies
    - Calculation of MRL
    - Establishment of withdrawal periods
    - Specific issues such as MRLs and residues at injection sites
- Pharmacokinetics and bioequivalence studies

  Data requirements to demonstrate bioequivalence of new products containing registered actives and new routes of administration are slightly different in various regional regulatory authorities, although the principles appear to be similar.

  Priority for harmonised Guidelines *(Would probably require a **new** Working Group)*:
    - Situations in which bioequivalence studies are appropriate
    - Design of bioequivalence studies, including statistical analysis of studies
- Common Technical Documentation

  Differences exist in the format, layout and requirements of Technical Documents in VICH regions.

  Priority for harmonised Guidelines *(Would probably require a **new** Working Group)*:
    - Content, technical requirements and format of technical documents
    - Quality assurance of technical document content
    - Technical assessment of document content
- Other Biological topics *(Could probably be dealt with by the **existing** Working Group)*:
    - Product classification and nomenclature

- Safety tests (including safety at injection site aned safety on reproductive system)
- Test of reversion to virulence
- In Vitro testing for killed products
- Batch release tests

- Safety and efficacy requirements for products for minor species *(Would probably require a **new** Working Group)*

III) Sustainability of Harmonisation (Goal 1.6 and 2)

The success of the VICH process will be **measured** by the rapid international acceptance of the VICH guidelines in the three member regions first, eventually by governments beyond those.
The international harmonisation process implies a **close follow-up** by all the participants, i.e. the Steering Committee participants, of the work already achieved by VICH i.e. the monitoring of the implementation of the GL and the eventual updating of adopted GL in order to address new scientific findings *(Goal 1.6)*.

The Steering Committee should therefore regularly dedicate a portion of its bi-annual meetings for participants to provide **reports on the implementation** and the uptake of VICH GL among their constituency (step 8 of step procedure). Specifically, regulatory authorities should notify, through the Secretariat, to the Steering Committee of the formal implementation. On the other hand, industry members (trade associations) should conduct surveys to objectively assess the harmonisation results.

Action: Authorities - Industry-All VICH members

VICH should furthermore monitor closely the **work programmes** of ICH, JECFA, OECD, WHO, OIE, ... in order to address sufficiently early new/emerging issues. In particular, VICH should evaluate the applicability of the each new ICH GL to the veterinary field.

VICH Steering Committee participants should furthermore be fully aware that they have a responsibility to monitor the activities of those other organisations with similar interests (e.g., ICH…) and to inform the Secretariat of relevant developments. The Secretariat is responsible for coordinating and facilitating the monitoring and reporting. The Steering Committee participants can require at any time from the Secretariat to put these new/emerging issues on the agenda of the next Steering Committee meeting.

Action: Steering Committee - Secretariat

IV) Communication (Goal 3)

VICH should have a **permanent communication policy** promoting world-wide the work and achievements of VICH. This will improve the international awareness of VICH guidelines. The communication with non-VICH countries through the OIE is an essential step to reach the ultimate goal of global harmonisation.

The **existing channels communication** channels should be developed and promoted:

- ***VICH Web site***: Divided in 8 different sectors/pages, the site defines VICH, presents the structure, explains the process, details the topics, gives direct access to draft and final guidelines, provides the names (and contact details for Steering Committee participants) of all the persons actively working in the VICH process, updates the visitor on recent news and meetings and finally provides the contact address for more info.

  Already proven very useful (...hits), the site needs more promotion, a regular (bi-monthly) update fine-tuning and further improvement.

  Action: Secretariat

- ***OIE***: Close collaboration with OIE during the **consultation process** in order to enable a broad participation to the VICH process; wide dissemination of the adopted guidelines and all relevant information through the OIE channel (paper, mail, link to web-site). OIE should communicate to the secretariat the timing of those consultations and provide the comments received.

Action: OIE collaborating centre

- ***VICH public Conferences***: public conferences should be held on a regular basis in order to increase the awareness of all interested parties (including the observers) as well as of the general public; the VICH Conferences should become a **forum for a permanent dialogue** between all interested parties. VICH public conferences should facilitate the exchange of information on new issues, avoid divergence of future requirements and accelerate the harmonisation of new technical requirements. The scheduling of the next VICH conference should therefore be set not less than 2 years nor more than 3 years after VICH1.

Action: Steering Committee

As **additional new communication channel**, Steering Committee participants should make a point of honour to communicate about the work of VICH through relevant international **publications** and during important international **meetings and events**.

Action: Steering Committee

A **liaison procedure with ICH, JECFA, OECD** should be put in place (see also above).

Action: Secretariat